IN THE SPECIFICATION:

Please replace the description of Figure 1 beginning on page 14, line 28, with the following rewritten description:

Oligonucleotides for assembling the gamma-crystalline mutants[[.]], which include CDLIE1B (SEQ ID NO: 1), GCLIE2P (SEQ ID NO: 11), GCLI3P (SEQ ID NO: 12), GCLIB4P (SEQ ID NO: 13), GCLI5P (SEQ ID NO: 14), GCLI6P (SEQ ID NO: 15), GCLIB7P (SEQ ID NO: 16), GCLI8P (SEQ ID NO: 17), GCLIE9P (SEQ ID NO: 18), GCLIE10 (SEQ ID NO: 2), and GCLIA11B (SEQ ID NO: 3).

Please replace the description of Figure 4 beginning on page 15, line 4, with the following rewritten description:

Oligonucleotides for amplifying the non-mutagenized region of gamma-II-crystalline[[.]], which include GCFORNOT (SEQ ID NO: 4) and GCBACKSfiBst (SEQ ID NO: 5).

Please replace the description of Figure 7 beginning on page 15, line 19, with the following rewritten description:

Partial DNA sequence of the BSA-estradiol-17-hemisuccinate-binding gamma-II-crystalline mutant 12A (Mu 12A; SEQ ID NO: 9) in phagemid pGCKT 8-3 and of gamma-II-crystalline wild-type (WT; SEQ ID NO: 10) in pCANTAB 5E respectively. The introduced cleavage sites Sfi I (5') and Bst EII (3') are indicated by italics and underlining. The codons of the randomized amino acid positions are in bold type.

Please replace the description of Figure 8 beginning on page 15, line 25, with the following rewritten description:

Derived amino acid sequences of the BSA-estradiol-17-hemisuccinate-binding gamma-II-crystalline mutant 12A (Mu 12A; SEQ ID NO: 19) and of gamma-II-crystalline wild-type (WT; SEQ ID NO: 20) after expression in the phagemids and removal of the signal peptide. The randomized amino acid positions are indicated by bold type and amino acids which have actually been exchanged are indicated

by bold type and are underlined. Amino acids additionally introduced at the N-terminals via the Sfi I cleavage site and the C-terminal E-tag fusion are shown in italics and underlined.

Please replace the description of Figure 9 beginning on page 16, line 1, with the following rewritten description:

Sequences of the primers used for cloning Mu 12A and gamma-II-crystalline into vector pET-20b[[.]], which include primers GC 20bbackWT (SEQ ID NO: 23), GC 20bback12A (SEQ ID NO: 24), and GC for 20b (SEQ ID NO: 25).

Please replace the description of Figure 10 beginning on page 16, line 4, with the following rewritten description:

Derived protein sequence of the BSA-estradiol-17-binding mutant 12A (SEQ ID NO: 21) and of bovine gamma-II-crystalline (SEQ ID NO: 22) after expression in pET-20b. The randomized amino acid positions are indicated by bold type and amino acids which have actually been exchanged are indicated by bold type and are underlined. C-terminal amino acids additionally introduced via the cloning, including the 6 histidine are shown in italics and underlined.

Stability of mutant 12A against the denaturing agent guanidine. The figure shows the emission maxima after incubating the purified mutant 12A (SEQ ID NO: 21) and gamma-II-crystalline (SEQ ID NO: 22) proteins with various concentrations of guanidine for various periods.

Please replace the description of Figure 11 beginning on page 16, line 11, with the following rewritten description:

Concentration-dependent binding of mutant 12A (SEQ ID NO: 21) to the BSA-beta-estradiol-17-hemisuccinate conjugate. The binding of the mutant (12A; SEQ ID NO: 21) and of gamma-II-crystalline (WT; SEQ ID NO: 22) to the conjugate (BSA-Estr. 17) and, as a control, to BSA was analysed.

Please replace the description of Figure 12 beginning on page 16, line 16, with the following rewritten description:

Stability of mutant 12A against the denaturing agent guanidine. The figure shows the emission maxima after incubating the purified mutant 12A (SEQ ID NO: 21) and gamma-II-crystalline (SEQ ID NO: 22) proteins with various concentrations of guanidine for various periods.

Please replace the description of Figure 13 beginning on page 16, line 21, with the following rewritten description:

Fluorescence emission spectrum of wild-type gamma-crystalline (SEQ ID NO: 22) and mutant 12A (SEQ ID NO: 21) in 50 mM Na phosphate, pH 6.5. The fluorescence signal (Fig. 13A) was measured at an excitation wavelength of 280 nm. The protein concentration was 100 µg/ml. Fig. 13B shows the absorbence spectra of the protein samples used for fluorescence measurement. The absorbence was determined in a cuvette with 1 cm path length.

Please replace the paragraph beginning on page 16, line 31, with the following rewritten paragraph:

The design of novel beta-sheet proteins with antigen-binding properties is shown on the basis of isolating a mutant of the bovine gamma-B-crystalline (gamma-II), which binds specifically to the hormone estradiol. Specific alteration of selected amino acid positions of a beta-sheet exposed on the surface produced a novel stable protein with beta-sheet structure and specific binding properties. After selecting the beta-sheet region or amino acids suitable for mutagenesis, a site-specific mutagenesis was carried out at the DNA level, and in a phagemid a beta-sheet mutant library was prepared, which makes expression and subsequent selection for novel binding properties of the mutants in the phage display system possible. The isolated mutant (SEQ ID NO: 19) was compared to the starting protein gamma-II-crystalline (SEQ ID NO: 20) with respect to its new properties.

Please replace the paragraph beginning on page 17, line 11, with the following rewritten paragraph:

Based on the X-ray structure of gamma-II-crystalline (Wistow et al., 1983), the N-terminal domain of gamma-II-crystalline (GENBANK® Accession[[.]] No. M16894) was selected for mutagenesis. Eight amino acids in all, which form a continuous surface segment, were identified there. The selected amino acids are part of a beta-sheet and should not contribute substantially to preserving the structure. They are amino acid positions which are accessible to the solvent and thus also to possible binding partners. The eight amino acids Lys [[2]]3, Thr [[4]]5, Tyr [[6]]7, Cys [[15]]16, Glu [[17]]18, Ser [[19]]20, Arg [[36]]37, and Asp [[38]]39 of SEQ ID NO: 22 comprise an area of approx. 6.1% of the total surface area of the protein.

Please replace the paragraph beginning on page 18, line 7, with the following rewritten paragraph:

All oligonucleotides used for assembling were adjusted to a concentration of 100 pmol/µl. First, the primers GCLIE1B (SEQ ID NO: 1) and GCLIE2P (SEQ ID NO: 11) were assembled. For this, 36 µl of washing and binding buffer (WB buffer: 1M NaCl, 10 mM Tris-HCl pH 7.5, 1 mM EDTA) were added to in each case 4 µl of the primers and the mixture was incubated at 70°C for 5 min. After assembly of the two primers and further incubation at 70°C for 5 minutes, the primer mixture was slowly cooled to room temperature. 4 µl of the GCLIE1B/GCLIE2P primer hybrids were mixed with 56 µl of WB buffer and added to 300 µg of the streptavidin-loaded MBs which had been washed beforehand with washing and binding buffer. Incubation at room temperature for 15 minutes was followed by washing the MBs with WB buffer and TE buffer (10 mM Tris-HCl pH 7.5, 1 mM EDTA). A primer linker fragment is added to the MBs coupled to the first primer hybrid, which fragment is prepared as follows: 4 µl of primer GCLIB4P (SEQ ID NO: 13) or GCLI5P (SEQ ID NO: 14) are mixed with 36 µl of 1 x ligation buffer from GIBCO BRL (50 mM Tris-HCl pH 7.6, 10 mM $MgCl_2$, 1 mM ATP, 1 mM DTT, 5% (w/v) polyethylene glycol-8000). After incubation at 70°C for 5 minutes, both mixtures are combined, incubated at 70°C for a further 5 min and cooled to room temperature. After adding 12 units of T4 DNA ligase (GIBCO BRL) and 8 µl of 1 x ligation buffer, the

reaction mixture is incubated at room temperature for 1 h. 12 µl of this GCLIE3P/GCLIB4P/GCLI5P bridging fragment are admixed with 54 µl of 1 x ligation buffer and 6 units of ligase, and the mixture is added to the washed MBs containing the first primer hybrid and incubated at room temperature for 1 h. After the ligation reaction, the MBs are washed twice with TE buffer and taken up in 64 µl of 1 x ligation buffer containing 8 µl of ligase. 8 µl of the assembled primer mixture GCLI6P (SEQ ID NO: 15)/GCLIB7P (SEQ ID NO: 16), which primers have been assembled beforehand in analogy to those of GCLIB4P/GCLI5P, were then added to the MBs. The ligation was again carried out at room temperature for 1 h. After washing the MBs twice in TE buffer, 12 µl of the 2nd bridging fragment GCLIB8P (SEQ ID NO: 17)/GCLIE9P (SEQ ID NO: 18)/GCLIE10 (SEQ ID NO: 2) are added and the mixture is ligated for 1 h. The 2nd bridging fragment is prepared analogously to the first bridging fragment, GCLIE9P (SEQ ID NO: 18) and GCLIE10 (SEQ ID NO: 2) being assembled first and then ligated with GCLI8P in the second step. The MBs with the immobilized primers are then again washed with TE buffer. The subsequent DNA-polymerase and ligase reaction fills in the gaps in the second strand. The MBs are incubated at 37°C for 30 min in the following buffer mixture: 52.5 µl of H_2O, 6 µl of buffer L from Boehringer (100 mM Tris-HCl pH 7.5, 100 mM $MgCl_2$, 10 mM dithioerythritol), 0.5 µl of dNTPs (25 mM of each dNTP) and 1 µl (2 units) of Klenow fragment (Boehringer). Washing the MBs twice with TE buffer is followed by the ligation reaction at room temperature for 1 h. A 100 µl mixture contains 10 units of ligase. After two washing steps with TE buffer, the DNA strand non-covalently bound to the MBs is removed by treatment with 40 µl of 0.1 M NaOH for 30 s, and the MBs are resuspended in 60 µl of TE. The PCR for amplifying the library is carried out using the MBs as template. The PCR reaction mixture (50 µl) is prepared as follows: 6 µl of MBs, 5 µl of 10 x PCR reaction buffer from Stratagene (100 mM KCl, 100 mM $(NH_4)_2SO_4$, 200 mM Tris-HCl pH 8.75, 20 mM $MgSO_4$, 1% Triton X-100, 1 mg/ml BSA), 1 µl (2,5 units) of Pfu DNA polymerase (Stratagene), 0.5 µl of dNTPs (25 mM of each dNTP), 0.35 µl of GCLIE1B (SEQ ID NO: 1). 0.35 µl of GCLIA11B (SEQ ID NO: 3) and 36.8 µl of H_2O. The PCR was carried out in 35 cycles with primer annealing at 55° for 1 min, a polymerase reaction at 72°C for 1.5 min, denaturation at 95°C for 1 min and a final polymerase reaction at 72°C for 5 min.

Please replace the two consecutive paragraphs beginning on page 19, line 19, with the following rewritten paragraphs:

Starting from phagemid pCANTAB 5E (PRAS kit from Pharmacia Biotech), a phagemid derivative for cloning the gamma-II-crystalline mutant band was thus constructed. The entire 3' region of gamma-II-crystalline (C-terminal domain; GENBANK Accession No. M16894) and the non-mutagenized 5' region were amplified by means of PCR using plasmid pGII (Mayr et al., 1994) as template and primers GCFORNOT (SEQ ID NO: 4) and GCBACKSfiBst (SEQ ID NO: 5; *see* Figs. 3, 4).

The Sfi I (GCBACKSfiBst; SEQ ID NO: 5) and Not I (GCFORNOT; SEQ ID NO: 4) cleavage sites introduced by the primers make insertion of the PCR product into phagemid (GCFORNOT; SEQ ID NO: 4) pCANTAB 5E possible. Together with the GCBACKSfiBst (SEQ ID NO: 5) primer, a Bst EII cleavage site was additionally integrated into the gamma-crystalline gene, which allowed cloning of the mutated gamma-crystalline DNA fragments. *de novo* introduction of the cleavage site does not alter the amino acid sequence in gamma-II-crystalline. After sequencing, the PCR product was cloned as Sfi I/Not I fragment into phagemid Sfi I/Not I cut with pCANTAB 5E. The phagemid pGCKT8-3 constructed in this way was the starting point for preparing the gamma-II-crystalline phage display library.

Please replace the paragraph beginning on page 20, line 28, with the following rewritten paragraph:

In control experiments, gamma-II-crystalline DNA was amplified using primers GCFORNOT (5' GAGTCATTCTGCGGCCGCATAAAAATCCATCACCCGTCTTAAA GAACC 3'; SEQ ID NO: 4) and GCBACKSFI (5' CATGCCATGACTCGCGGCCC AGCCGGCCATGGGGAAGATCACTTTTTACGAGGAC 3'; SEQ ID NO: 6) and plasmid pGII (Mayr et al., 1994) as template. After cleavage with Not I and Sfi I restriction endonucleases, the sequenced PCR product was cloned into the Sfi I/Not I phagemid likewise cut with pCANTAB 5E.

Please replace the paragraph beginning on page 24, line 13, with the following rewritten paragraph:

80 individual clones were selected from the bacterial clones obtained after the 3rd panning. Phages were isolated from the clones and assayed individually in the monoclonal phage ELISA with respect to their antigen binding. Individual bacterial clones were cultivated in 100 µl of 2 × YT medium containing 2% glucose and 100 µg/ml ampicillin in polypropylene microtitre plates (NUNC) with gentle agitation (100 rpm) overnight. 2 µl of these bacterial cultures were diluted 1:100 in the same medium and cultured at 100 rpm at 37°C to an OD_{600} of 0.4. Phages were obtained as described for the selection process. Deep well polypropylene microtitre plates from TECAN were used for phage cultivation. For the ELISA, 200 µl of the phage supernatant obtained after centrifugation (not concentrated) were blocked with 40 µl of 6x_PBS/18% at room temperature for 1 h. 30 out of 80 clones assayed showed significant binding of the recombinant phages to BSA -Estradiol-17 and not to BSA assayed in parallel. Phages with wild-type gamma-II-crystalline showed in a control experiment no binding to BSA-estradiol-17 whatsoever. 14 selected binding phages were sequenced using the IRD 800-labelled primers pCANR1LAB (5' CCATGATTACGCC[[-]]AAGCTTTGGAGCC 3'; SEQ ID NO: 7) and GCLISEQ (5' CTGAAAGTGCCGGTGTGTTGC 3'; SEQ ID NO: 8). Only in one case, sequencing revealed a gamma-crystalline variant (Mu 12A) which was mutated exclusively in the eight randomized amino acid positions. A number of clones showed shifts in the reading frame and, although theoretically coding for a functional protein, had alterations which were not exclusively in the expected gamma-crystalline region. These frame shift mutants were not studied further.

Please replace the paragraph beginning on page 25, line 3, with the following rewritten paragraph:

Expression of the fusion protein Mu 12A-minor coat protein 3 on the surface of the recombinant phages and expression of Mu 12A in *E. coli* strain HB 2151 were detected by means of Western-blot analyses using the anti-G3P and anti-E-Tag antibodies (Pharmacia-Biotech), respectively. The DNA sequences of mutant 12A (SEQ ID NO: 9) in ~~phageimid~~ phagemid pGCKT 8-3 and of gamma-II-crystalline wild-type (SEQ ID NO:

10) are depicted in Fig. 7. The DNA sequence starts at the Sfi I cleavage site which is already present in the starting phageimid pCANTAB 5E and ends, in the case of pGCKT 8-3, at the Bst EII site newly introduced into the gamma-II-crystalline gene and, in the case of the gamma-II-crystalline wild-type gene, at the original sequence. Fig. 8 depicts the amino acid sequences derived therefrom. Codon randomization at amino acid position 36 does not change the amino acid arginine at this position. Computer ~~modelling~~ modeling of mutant 12A (SEQ ID NO: 19) shows that the amino acid exchanges do not cause large alterations in the protein structure compared with the starting protein. However, the net charge becomes more positive.

Please replace the paragraph beginning on page 25, line 21, with the following rewritten paragraph:

In order to characterize mutant 12A in detail, the DNA (SEQ ID NO: 9) was recloned into plasmid pET-20b (Novagen). The plasmid makes possible a high expression of the recombinant DNA in *E. coli* strain BL 21 and simple purification of the foreign proteins. Genes are expressed here without signal peptide and with a C-terminal fusion of 6 histidine residues. The DNAs of mutant 12A (SEQ ID NO: 9) and of bovine gamma-II-crystalline wild-type (SEQ ID NO: 10) were amplified by means of PCR using the appropriate ~~phageimid~~ phagemid DNA and primers GC 20bback12A/GC (SEQ ID NO: 24) for 20b for mutant 12A and GC 20bbackWT/GC (SEQ ID NO: 23) for 20b for the wild-type (Fig. 9). The PCR fragments were cleaved with restriction endonucleases Nde I and Bam HI and cloned into vector pET 20b cut with Nde I/ Bam HI. Fig. 10 depicts the theoretical amino acid sequence of mutant 12 A (SEQ ID NO: 21) and of gamma-II-crystalline (SEQ ID NO: 22), respectively, after expression in pET-20b. The first 10 N-terminal amino acids of mutant 12 A (SEQ ID NO: 21) were confirmed by N-terminal protein sequencing.